The Rejection Under 35 U.S.C. § 112, First Paragraph Should Be Withdrawn

The Examiner has rejected claims 23-26 under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In particular, the Examiner alleges that the rejected claims are directed to a genus of DNA molecules and that the specification discloses only a single species, *i.e.*, SEQ ID NO. 2, of the claimed genus. Accordingly, the Examiner indicates that the disclosure is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Applicants respectfully disagree for the following reasons.

Applicants submit that the legal test for sufficiency of written description is whether the disclosure of the application reasonably conveys to the skilled artisan that the inventor had possession of the claimed subject matter. *In re Castle*, 707 F.2d 1366, 1375, 217 U.S.P.Q. (BNA) 1089, 1096 (Fed. Cir. 1983); *Vas-Cath Inc. v. Mazurka*, 935 F.2d 1555, 1563; *see also Ralston Purina Co. v. Far-Mar-Co, Inc.*, 772 F.2d 1570, 1575, 227 U.S.P.Q. (BNA) 177, 179 (Fed. Cir. 1985). Applicants direct the Examiner's attention to the Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, ¶1, "Written Description" Requirement, published January 5, 2001, Federal Register, Volume 66, Number 4, page 1106:

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species, by actual reduction to practice . . . or by disclosure of relevant identifying characteristics, *i.e.*, structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation

between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus.

Preliminarily, Applicants submit that contrary to the Examiner's indication that the specification only discloses a single species of the claimed genus, the specification provides a representative number of species of the genus, including the DNA molecules encoding polypeptides with an amino acid sequence of SEQ ID NO:2 or constitutively active variants with an amino acid substitution at the Serine at residue 207 or the Threonine at residue 211 with negatively charged amino acids such as glutamic acid or aspartic acid and constitutively inactive variants with an amino acid substitution at the Lysine at residue 69 (specification at page 6, line 31 to page 7, line 11). Based on the disclosure of such representative species, one skilled in the art would recognize the structural attributes and features characteristic of the claimed genus.

Applicants also submit that one skilled in the art would be able to "visualize or recognize the identity of the members of the genus" based on the additional teachings of the specification. Applicants need not disclose the complete specific structure of each and every isolated DNA molecules encoding a polypeptide 90% identical to SEQ ID NO:2 to satisfy the written description requirement. As provided *supra*, the legal standard for written description purposes is met if the specification discloses relevant identifying structural and functional characteristics sufficient to show that Applicants were in possession of the claimed genus. The structure of the genus is clearly premised on the teachings in the specification which provide a specific sequence, *i.e.* SEQ ID NO:2 which corresponds to the amino acid sequences encoding a MEK6 polypeptide or variant thereof. Based on the teachings of the specification with respect to variants, the claimed genus of proteins that are variants of SEQ

ID NO: 2 having at least 90% structural identity with the disclosed species are clearly defined in the instant specification such that one skilled in the art would recognize from the disclosure that Applicants were in possession of the genus of proteins that are variants of SEQ ID NO:2 with modifications at no more than a 10% of the amino acid residues (specification page 4, line 34 to page 6, line 6). Further, claims 24 and 26 require that the genus must be capable of a specified activity *i.e.*, have the capability to phosphorylate a substrate or have the incapability to phosphorylate a substrate. The specification describes variants of SEQ ID NO:2 which have 90% identity to SEQ ID NO: 2 and have the claimed capability of phosphorylating a substrate (see specification page 6, line 31 to page 7, line 2). Similarly, the specification describes variants of SEQ ID NO:2 which have 90% identity to SEQ ID NO: 2 and have the claimed incapability of phosphorylating a substrate (see page 7, lines 3-11). The procedures for making the variants of SEQ ID NO:2 are described in the specification (for example at specification page 6, lines 9-20) or known in the art and the assays for identifying all of the at least 90% identical variants of SEQ ID NO:2 which are capable of the specified activity, *e.g.,* capable of phosphorylating a substrate or incapable of phosphorylating a subtrate, are described in the specification and known in the art (see specification at page 8, lines 17-28). Indeed, procedures for making variants of SEQ ID NO:2 which have 90% identity to SEQ ID NO:2 that retain or lose the capability for phosphorylation of a substrate are described in the specification and known in the art. Accordingly, one skilled in the art would conclude that Applicants were in possession of the necessary common attributes possessed by members of the genus.

In view of the foregoing, Applicants respectfully submit that the written description requirement has been met for claims 23-26 and that the rejection under 35 U.S.C. § 112, first paragraph should be withdrawn.

The Rejection Under 35 U.S.C. § 112, First Paragraph Should Be Withdrawn

The Examiner has rejected claims 23-26 under 35 U.S.C. § 112, first paragraph, as lacking enablement. In particular, the Examiner alleges that the specification, while being enabling for the MEK6 of SEQ ID NO: 2, does not reasonably enable a MEK with structures different from SEQ ID NO: 2; and the specification does not provide sufficient enablement of a polypeptide of unknown function. Applicants respectfully disagree and submit that under the legal test for enablement one skilled in the art could make and use the claimed invention, without undue experimentation, from the disclosure in the patent specification coupled with information known in the art at the time the patent application was filed. *U.S. v. Telectronics Inc.*, 857 F.2d 778, 8 U.S.P.Q.2d 1217 (Fed. Cir. 1988). Applicants respectfully submit that the Examiner has not provided conclusive evidence contrary to the teachings of the specification and state of the art.

Applicants submit that recombinant and mutagenesis techniques are known in the art and that it would be routine in the art to make the claimed polypeptide variants of MEK6. Furthermore, it would be routine to screen for variant sequences with the specified activity. Applicants direct the Examiner's attention to the specification which provides representative assays which can evaluate the effect of any modification made in MEK6. For example, page 6, line 31 to page 7, line 11 describe modifications made and methods for evaluating the effect of any modification on the polypeptide function or activity. In particular, Applicants direct the Examiner's attention to the specification at page 8, lines 18-28 of the specification.

Applicants cannot agree with the Examiner's conclusion without references or reasonable scientific explanations with respect to why the specification and standard techniques known in the art would not be adequate for one skilled in the art to make and use

the claimed invention without undue experimentation. Applicants submit that guided by the specification and techniques known in the art, one skilled in the art could successfully make modified polypeptides and assay them for effect of such modifications using the representative assays provided in the specification or known in the art. Indeed, Applicants submit that not only does the specification provide sufficient guidance as to which modifications are likely to be successful for the desired activity, but also that the assays and methods for evaluating modifications of polypeptides, as encompassed by the instant claims, are known in the art and can be readily performed by the skilled artisan without undue experimentation. Arguably, there might be considerable experimentation. However, even if it were true that the experimentation might be time-consuming or complicated, it would only be undue experimentation if the experimentation would require a level of ingenuity beyond what is expected from one of ordinary skill in the field. *Fields v. Conover,* 170 U.S.P.Q. 276, 279 (C.C.P.A. 1971). As discussed *supra* this is not the case where one skilled in the art would require ingenuity to practice the claimed invention given the teachings of the specification. Furthermore, a considerable amount of experimentation is permissible, so long as it is merely routine. *In re Certain Limited-Charge Cell Culture Microcarriers*, 221 U.S.P.Q. 1165, 1174 (Int'l Trade Comm'n 1983), *aff'd. sub nom.*, *Massachusettts Institute of Technology v. A.B. Fortia* 774 F.2d 1104,227 USPQ 428 (Fed. Cir. 1995).

With respect to claim 25, the Applicants further submit that claim 25 further recites that the isolated DNA molecule encode a constitutively active polypeptide. In view of the teachings of the specification at page 6, line 25 to page 7, line 2 and standard mutagenesis techniques known in the art, the DNA molecules claimed in claim 25 are clearly enabled. One skilled in the art would be able to make modifications using standard techniques and

assay the molecules for constitutive activity using assays for MEK6 kinase activity described in the specification.

With respect to claim 26, the Applicants further submit that claim 26 further recites that the isolated DNA molecule encode a constitutively inactive polypeptide. In view of the teachings of the specification at page 7, line 3, lines 3-11 and standard mutagenesis techniques known in the art, the DNA molecules claimed in claim 26 are clearly enabled. One skilled in the art would be able to make modifications using standard techniques and assay the molecules for the loss of ability to activate substrate using assays for MEK6 kinase activity described in the specification.

In view of the foregoing, Applicants submit that the rejection of claims 23-26 under 35 U.S.C. § 112, first paragraph should be withdrawn.

The Rejections Under 35 U.S.C. § 112, Second Paragraph Should Be Withdrawn

The Examiner has claims 25-26 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular, the Examiner objects to claims 25-26 in that claim 25 recites the phrase "constitutively active" and claim 26 recites the phrase "constitutively inactive." The Examiner alleges that the claims are rendered indefinite because the claims could refer to many polypeptides with different activities such as immunological activity or enzymatic activity. The Examiner concludes that the scope of the polypeptides claimed is unclear.

Contrary to the Examiner's position, Applicants respectfully submit that the one skilled in the art would understand the scope of the phrase "constitutively active" or "constitutively inactive"and that the scope of the claims is clear because the specification

provides a definition of each phrase at page 6, lines 31 to 34 and at page 7, lines 3 to 4, respectively. "Constitutively active" polypeptides display the ability to stimulate p38 phosphorylation in the absence of stimulation by cytokines, UV, stress-inducing agents or osmotic shock. "Constitutively inactive" polypeptides display the lack of such ability to stimulate p38 phosphorylation when stimulated as described above.

In view of the foregoing, Applicants submit that the scope of claims 25-26 is clear and request that the rejection of claims 25-26 under 35 U.S.C. § 112, second paragraph be reconsidered and withdrawn.

The Rejection Under 35 U.S.C. § 102 Should Be Withdrawn

The Examiner has rejected claims 1 and 23-26 under 35 U.S.C. § 102(e) as being anticipated by Davis *et al.* (U.S. Patent No. 5,736,381) made of record. In response, Applicants submit that Davis *et al.* is not applicable as a prior art reference. Applicants submit herewith a Declaration of the Inventors under 37 C.F.R. §1.131 (hereafter "the Declaration") accompanied by Exhibit A. As part of the Declaration, the Inventors state that they possessed the claimed invention prior to September 19, 1995, which is evidenced by the accompanying Exhibit A which documents possession of the claimed invention prior to September 19, 1995. Accordingly, the Applicants possessed the claimed invention of the present application prior to September 19, 1995, which is the effective date of Davis *et al.* Because Davis *et al.* was not issued as a U.S. Patent or filed more than one year before the filing date of the present Application and the Inventors possessed the claimed invention prior to the filing date of the Davis *et al.* patent, Davis *et al.* cannot be properly cited as prior art for the Examiner's rejection under 35 U.S.C. §102(e). Therefore, in view of the submission

of the Declaration, Applicants respectfully submit that the Examiner's rejection should be withdrawn.

The Rejection Under 35 U.S.C. § 103(a) Should Be Withdrawn

The Examiner has rejected claims 1 and 22 as being unpatentable over Davis *et al.* in view of Smith (U.S. Patent No. 5,654,176) under 35 U.S.C. § 103(a). Applicants submit that in view of the submission of the Declaration showing invention prior to September 19, 1995, Davis *et al.* is no longer available as a proper prior art reference for the Examiner's rejection under 35 U.S.C. § 103(a), see discussion *supra.* Further, Applicants submit that Smith is directed to a fusion protein comprising glutathione-S-transferase and does not disclose any polypeptides with an amino acid sequence of SEQ ID NO:2. Accordingly, Applications respectfully submit that the Examiner's rejection under 35 U.S.C. § 103(a) should be withdrawn.

Double Patenting

The Examiner has rejected claims 23-26 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-2 of U.S. Patent No. 6,074,862. With respect to the rejection of claims 23-26, Applicants request that this rejection be held in abeyance until such time as allowable subject matter is indicated.

CONCLUSION

Applicants respectfully request that the amendments and remarks of the present response be entered and made of record in the instant application, and that the Examiner reconsider the rejections in view of these amendments and remarks. Accordingly,

after entry of this Amendment, all of the pending claims should be in condition for allowance. Withdrawal of the rejections and allowance of all the claims is earnestly requested.

Applicants respectfully request that the Examiner call Anthony M. Insogna at (212) 790-9090 if any questions or issues remain.

Respectfully submitted,

Date March 21, 2002

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Enclosure